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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>A61K 7/50</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 95/32705</b> <b>(43) International Publication Date:</b> 7 December 1995 (07.12.95)
<b>(21) International Application Number:</b> PCT/EP95/01944 <b>(22) International Filing Date:</b> 22 May 1995 (22.05.95) <b>(30) Priority Data:</b> 08/252,298 1 June 1994 (01.06.94) US <b>(71) Applicant (for AU BB CA GB IE KE LK MN MW NZ SD SG SZ TT UG only):</b> UNILEVER PLC [GB/GB]; Unilever House, Blackfriars, London EC4P 4BQ (GB). <b>(71) Applicant (for all designated States except AU BB CA GB IE KE LK MN MW NZ SD SG SZ TT UG):</b> UNILEVER N.V. [NL/NL]; Weena 455, NL-3013 AL Rotterdam (NL). <b>(72) Inventors:</b> FUJITWARA, Mitsuko; 602 Nelson Court, Edgewater, NJ 07020 (US). VINCENT, Carol; 18 Wolfe Drive, Wanaque, NJ 07465 (US). ANANTHAPADMANABHAN, Kavssery; 186 Temple Hill Road #1905, New Windsor, NY 12533 (US). VILLA, Virgilio; 140 Grove Street, Bergenfield, NJ 07621 (US). <b>(74) Agent:</b> BRYANT, Tracey; Unilever plc, Patent Division, Colworth House, Sharnbrook, Bedford MK44 1LQ (GB).		<b>(81) Designated States:</b> AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).  <b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> MILD ANTIMICROBIAL LIQUID CLEANSING FORMULATIONS  <b>(57) Abstract</b>  The present invention relates to liquid skin cleansing compositions comprising (1) mild surfactant systems; (2) 0.1 to 10 % by wt. of a compound or compounds which buffer the pH of the composition; and (3) 1 % to 99 % water to potentiate the bactericidal activity. In a second embodiment of the invention, the buffering compound or compounds potentiates antibacterial effect in compositions already containing an antibacterial agent.		

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MILD ANTIMICROBIAL LIQUID CLEANSING FORMULATIONSBACKGROUND OF THE INVENTION

5 The present invention relates to liquid cleansing compositions having enhanced antimicrobial effectiveness. More specifically, the invention relates to a compound or compounds which potentiate the antimicrobial activity of liquid cleaning formulations by buffering the pH of the  
10 formulation such that the pH will rise no higher than 5.5, preferably between 2.5 to 5.5 under in use conditions (as opposed to initial pH).

15 There is a large demand in the market for mild liquid cleansing formulations which additionally have an antibacterial effect. Antibacterial cleansers are preferred because they kill germs and mild personal cleansers are preferred to minimize skin irritation, dryness etc. However, the combination of mild cleansing formulations and strong  
20 antimicrobial effect is difficult to achieve. Thus, for example, while soaps provide antibacterial effects, they are not mild to the skin. When very mild non-soap surfactants are used, antibacterial effect is greatly compromised.

25 The balancing act between providing mildness and effective antibacterial effectiveness is recognized for example in International Publication WO 92/18100. In this publication, improved clinical mildness is said to be provided through the use of a water soluble cationic polymer (see page 10, lines  
30 24-29). Cationic polymer is apparently used instead of additional ethoxylated surfactant because the percent of ethoxylated mildness surfactant must be minimized in order not to affect antimicrobial effectiveness (page 7 lines 4-6).

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Another approach to providing mildness effect without affecting antibacterial properties is that which appears to be used by Dial in, for example, Liquid Dial Plus with Moisturizers Antibacterial Soap®. Here, mildness benefits are apparently provided by the use of moisturizing compounds rather than by the use of very mild surfactants alone which, as indicated above, compromise antibacterial effectiveness.

In both cases, it can be readily seen that it is extremely difficult to provide effective antibacterial action in the presence of very mild surfactants. Rather, it is necessary to minimize the presence of those mild surfactants, to use larger amounts of harsher surfactants or soaps and to mask the effects of the harshness by providing cationic mildness conditioning agents (WO 92/18100) or moisturizers (as in the Dial product).

It would be greatly beneficial if antibacterial effectiveness could be provided either by providing a compound or compounds which alone or together buffer pH of a liquid composition at a pH low enough to provide antibacterial effectiveness for that composition formulation; or by providing a compound or compounds which alone or together buffer pH of a liquid composition containing anti-bacterial agent thereby enhancing (i.e., potentiating) the effect of the antibacterial agent even in compositions with very mild surfactant systems.

Fatty acids and their ester derivatives have been used to provide antimicrobial effectiveness in foods, pharmaceuticals and cosmetics (see, for example EP 0,244,144; US 4,002,775; US 4,406,884; US 4,997,851 and Kabara in JAOCS, vol. 61 No. 2, (February, 1984)).

The use of short chain fatty acids generally as potentiators of germicides is also known. These fatty acids, for example,

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have been used as potentiators with halogenated germicides at high pH and with isethiazolones (see FR 2,223,049 and EP 488,606).

5 US 3,218,260 to Lewandowski discloses cleaner compositions containing various organic or inorganic acids. The pH of these compositions (less than 2) is well below the pH of the skin cleansing compositions of the present invention.

10 In none of these references is it taught or suggested that one or more compounds be used either to enhance antibacterial effect in liquid skin cleansing compositions or to potentiate antibacterial compounds which may already be present in liquid skin cleansing compositions at the pH specified by the  
15 claims of the subject invention.

US Patent No. 5,132,037 to Greene et al teaches aqueous compositions in which C<sub>8</sub>-C<sub>22</sub> free fatty acids may be used. All examples (palmitic, stearic) are clearly directed to  
20 longer chain fatty acids and there is absolutely no recognition of the antibacterial or potentiating effect of lower chain fatty acids.

Unexpectedly, applicants have now found that one or more  
25 compounds (e.g., short chained fatty acids, hydroxy acids and polymeric acids) may be used to buffer the pH of a composition to within a defined low pH range and to therefore:

30 (1) enhance the antibacterial effect of liquid skin cleansing compositions; and/or

(2) potentiate the antibacterial effect of liquid skin cleansing compositions which already contain an  
35 antibacterial agent.

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**BRIEF SUMMARY OF THE INVENTION**

The present invention relates to liquid skin cleansing compositions comprising:

- (1) any mild surfactant system (i.e., any one or more surfactants which alone or together are demonstrated by clinical tests (eg zein test) to be milder than soap itself) in an amount of from about 1-99 wt%, preferably 2-85 wt%, more preferably 3-40 wt%;
- (2) 0.1 to 10%, preferably 0.1 to 5%, more preferably 0.5 to 5.0 wt% of a compound or compounds which alone or together buffer the pH of the liquid skin cleansing composition such that the pH is no higher than 5.5 under in-use conditions (i.e., 1:0.5 to 1:100 dilution, preferably 1:1 to 1:25 dilution of product in H<sub>2</sub>O); and
- (3) 1 to 99 wt%, preferably 15 to 97, most preferably 60 to 97 wt% water.

In a second embodiment of the invention, the liquid skin cleansing composition further comprises 0.001 to 5 wt% of an antibacterial agent and the buffering compound or compounds act to potentiate the antimicrobial/antibactericidal effect of the composition.

**DETAILED DESCRIPTION OF THE INVENTION**

The present invention relates to liquid skin cleansing compositions comprising 1 to 99, preferably 2 to 85, more preferably 3 to 40 wt% of a mild surfactant system comprising one or more surfactants which alone or together have been clinically tested to be milder than soap itself as measured by zein solubilization test (soap yields 80% zein

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solubilized). Preferably, the mildness is such that zein solubilization is in the range 10-60% solubilization.

5 A number of anionic, nonionic, cationic and amphoteric surfactants may be employed in the surfactant system of the invention provided of course that the surfactant, if used alone, or surfactant mixture is milder than would be soap itself as measured by the zein solubilization test.

10 Among suitable anionic coactives are the alkyl ether sulfates, acyl isethionates, alkyl ether sulfonates, sarcosinates, sulfosuccinates, taurates and combinations thereof. Among suitable amphoteric co-actives may be  
15 included alkylbetaines, amidopropyl betaines, amidopropyl sultaines and combinations thereof.

Alkyl ether sulfates will be of the general formula R-  
(OCH<sub>2</sub>CH<sub>2</sub>)<sub>n</sub>OSO<sub>3</sub>-M<sup>+</sup> wherein R ranges from C<sub>8</sub>-C<sub>20</sub> alkyl, preferably C<sub>12</sub>-C<sub>15</sub> alkyl, n is an integer from 1 to 40, preferably from 2  
20 to 9, optimally about 3, and M<sup>+</sup> is a sodium, potassium, ammonium or triethanolammonium cation.

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Typical commercial coactives of this variety are listed in the Table below:

Trademark	Chemical Name	Physical Form	Manufacturer
Steol CS 330	Sodium Laureth Sulfate	Liquid	Stepan
Standopol ES-3	Sodium Laureth Sulfate	Liquid	Henkel
Alkasurf ES-60	Sodium Laureth Sulfate	Paste	Alkaril
Cycloryl TD	TEA Laureth Sulfate	Paste	Cyclo
Standapol 125-E	Sodium Laureth-12 Sulfate	Liquid	Henkel
Cedepal TD407MF	Sodium Trideceth Sulfate	Paste	Miranol
Standopol EA-2	Ammonium Laureth Sulfate	Liquid	Henkel

Alkyl ether sulfonates may also be employed for the present invention. Illustrative of this category is a commercial product known as Avenel S-150 commonly known as a sodium C<sub>12</sub>-C<sub>15</sub> Pareth-15 sulfonate.

Another coactive type suitable for use are the sulfosuccinates. This category is best represented by the monoalkyl sulfosuccinates having the formula RO<sub>2</sub>CCH<sub>2</sub>CH(SO<sub>3</sub>-Na<sup>+</sup>)COO-M<sup>+</sup>; and amido-MEA sulfosuccinates of the formula: RCONHCH<sub>2</sub>CH<sub>2</sub>O<sub>2</sub>CCH<sub>2</sub>CH(SO<sub>3</sub>-M<sup>+</sup>)COO-M<sup>+</sup>; wherein R ranges from C<sub>8</sub>-C<sub>20</sub> alkyl, preferably C<sub>12</sub>-C<sub>15</sub> alkyl and M<sup>+</sup> is a sodium, potassium, ammonium or triethanolammonium cation. Typical commercial products representative of these co-actives are those listed in the Table overleaf:



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Trademark	Chemical Name	Physical Form	Manufacturer
Emcol 4400-1	Disodium Lauryl Sulfosuccinate	Solid	Witco
Witco C5690	Disodium Cocoamido MEA Sulfosuccinate	Liquid	Witco
McIntyre Mackanate CM40F	Disodium Cocoamido MEA Sulfosuccinate	Liquid	McIntyre
Schercopol CMSNa	Disodium Cocoamido MEA Sulfosuccinate	Liquid	Scher
Emcol 4100M	Disodium Myristamido MEA Sulfosuccinate	Paste	Witco
Schercopol	Disodium Oleamido MEA	Liquid	Scher
Varsulf S13333	Disodium Ricinoleamido MEA Sulfosuccinate	Solid	Scherex

Sarcosinates may also be useful in the present invention as a coactive. This category is indicated by the general formula  $RCON(CH_3)CH_2CO_2-M^+$ , wherein R ranges from  $C_8$ - $C_{20}$  alkyl, preferably  $C_{12}$ - $C_{15}$  alkyl and  $M^+$  is a sodium, potassium ammonium or triethanolammonium cation. Typical commercial products representative of these co-actives are those listed in the Table below:

Trademark	Chemical Name	Physical Form	Manufacturer
Hamosyl L-95	Sodium Lauroyl Sarcosinate	Solid	W. R. Grace
Hamosyl TOC-30	TEA Cocoyl/ Sarcosinate	Liquid	W. R. Grace

Taurates may also be employed in the present invention as a coactives. These materials are generally identified by the formula  $RCONR'CH_2CH_2SO_3-M^+$ , wherein R ranges from  $C_8$ - $C_{20}$  alkyl, preferably  $C_{12}$ - $C_{15}$  alkyl,  $R'$  ranges from  $C_1$ - $C_4$  alkyl, and  $M^+$  is a sodium, potassium, ammonium or triethanolammonium cation.

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Typical commercial products representative of these co-actives are those listed in the Table below:

Trademark	Chemical Name	Physical Form	Manufacturer
Igepon TC42	Sodium Methyl Cocoyl Taurate	Paste	GAF
Igepon T-77	Sodium Methyl Oleoyl Taurate	Paste	GAF

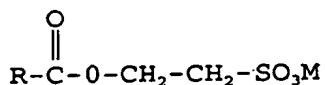
Within the category of amphoterics there are three general categories suitable for the present invention. These include alkylbetaines of the formula  $RN^+(CH_2)_2CH_2CO_2-M^+$ , amidopropyl betaines of the formula  $RCONHCH_2CH_2CH_2N^+(CH_2)_2CH_2CO_2-M^+$  and amidopropyl sultaines of the formula  $RCONHCH_2CH_2N^+(CH_2)_2CH_2SO_3-M^+$  wherein R ranges from  $C_8-C_{20}$  alkyl, preferably  $C_{12}-C_{15}$  alkyl, and  $M^+$  is a sodium, potassium, ammonium or triethanolammonium cation. Typical commercial products representative of these co-actives are those found in the Table below:

Trademark	Chemical Name	Physical Form	Manufacturer
Tegobetaine F	Cocamidopropyl Betaine	Liquid	Goldschmidt
Lonzaine C	Cocoamidopropyl Betaine	Liquid	Lonza
Lonzaine CS	Cocoamidopropyl Hydroxysultaine	Liquid	Lonza
Lonzaine 12C	Coco-Betaine	Liquid	Lonza
Schercotaine MAB	Myristamidopropyl Betaine	Liquid	Lonza
Velvetex OLB-50	Oleyl Betaine	Paste	Henkel

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Within the broad category of liquid co-actives, the most effective are the alkyl sulfates, alkyl ether sulfates, alkyl ether sulfonates, sulfosuccinates, and amidopropyl betaines.

Another preferred surfactant is an acyl isethionate having the formula:



in which R denotes a linear or branched alkyl group and M denotes an alkali metal or alkaline earth metal or an amine.

Other surfactants which may be used are the monoalkyl or dialkylphosphate surfactants.

Yet another mild surfactant which may be used, preferably as the primary surfactant in combination with the coactives noted above, is sodium coco glyceryl ether sulfonate (sodium coco AGS). While desirable to use because of its mildness properties, this coco AGS alone does not provide optimum lather creaminess. A sodium 90/10 coconut/tallow alkyl AGS distribution is preferred for creaminess. Salts other than the sodium salt, such as TEA-, ammonium, and K-AGS, and chain length distributions other than 90/10 coconut/tallow are usable at moderate levels. Also, some soap may be added to improve lather volume and speed of lathering. Certain secondary co-surfactants used in combination with AGS can also provide a creamier and more stable lather. These secondary surfactants should also be intrinsically mild. One secondary surfactant that has been found to be especially desirable is sodium lauroyl sarcosinate (e.g. Hamposyl L, made by Hampshire Chemical).

The amphoteric betaines and sultaines noted above can be used as the sole surfactant, but are more preferred as a co-surfactant or coactive. Nonionics generally should not be

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used as the sole surfactant in this product if high forming is desirable; however, they can be incorporated as a co-surfactant.

5 Nonionic and cationic surfactants which may be used include any one of those described in US Patent No. 3,761,418 to Parran, Jr., incorporated herein by reference.

10 Soaps can be used at levels of about 1-10%. Soaps can be used at higher level provided that the surfactant mixture is milder than soap. The soaps may be added neat or made in situ by adding a base, e.g., NaOH; to free fatty acid.

15 Of course, as noted above, soaps should only be used as cosurfactants to the extent that the surfactant system is milder than soap alone.

20 A preferred surfactant active system is one such that acyl isethionate comprises 1 to 15% by weight of the total composition, an anionic other than acyl isethionate (e.g., ammonium lauryl ether sulfate) comprises 1 to 15% by weight of the total composition and an amphoteric comprises 0.5 to 15% by weight of the total composition.

#### 25 BUFFERING COMPONENT

30 The second essential component of the liquid composition of the invention is the compound or compounds which alone or together buffer the pH of the formulation under in-use conditions such that the pH is up to 5.5, preferably from 2.5 up to 5.5, most preferably from 3.5 to less than 5.0.

By in-use is meant dilution of 1:0.5 to 1:100, preferably 1:1 to 1:25, of the product in water during use.

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This compound or compounds can be any organic acid or organic acid anhydride (including polymeric organic acids and anhydrides) or inorganic acid, which lowers the pH of the compositions in use preferably from 2.5 up to 5.5 and buffers at this pH.

Examples of inorganic acids which may lower pH and buffer at this pH are phosphoric acid and carbonic acid. Examples of organic acids and their anhydrides include carboxylic acids, hydroxy carboxylic acids and polymeric acids. A polymeric acid is a polymer containing carboxylic acid or a carboxylic acid anhydride with a weight average molecular weight of at least 3000 and a mole% carboxyl functionality of at least 40%. Examples of suitable materials include polyacrylic acids, polymethacrylic acids and pectic acids and mixtures thereof.

Preferred organic compounds buffering at low pH are short chain fatty acids. The fatty acid may be a substituted or unsubstituted, saturated or unsaturated fatty acids having a chain length of  $C_2$ - $C_{18}$ , preferably  $C_4$ - $C_{10}$ . While not wishing to be bound by theory, it is believed that longer chain lengths function better with increased solubility (e.g., higher substitution). In general, however, lower chain lengths are preferred. The fatty acid will generally comprise about 0.1% to 10% by weight of the composition.

Another class of organic acid which may be used are the hydroxy carboxylic acids. This includes any organic compound having at least one carboxylic acid group and at least one hydroxyl group. Preferably, the chain length of the acid should be  $C_2$  to  $C_{18}$ , preferably  $C_2$  to  $C_{12}$ . The many acids which may be used include citric acid, lactic acid, glycolic acid,  $\alpha$ -hydroxy  $C_8$  acid,  $\alpha$ -hydroxy  $C_{16}$  acid, acylated citric acid and  $\beta$ -hydroxybutyric acid. Lactic acid is particularly preferred.

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In a second embodiment of the invention, the liquid skin  
cleansing compositions of the subject invention comprise an  
antibacterial agent. In this embodiment of the invention, the  
buffering compound or compounds described above not only may  
5 provide antibacterial effect on its own, but also enhances  
(potentiates) the antibacterial effectiveness of the  
antibacterial agent.

The antibacterial agent can be present at a level of from  
10 about 0.001% to about 5%, typically from 0.01% to 2%, and  
preferably from 0.01% to 1.5 wt% of the composition. The  
level is selected to provide the desired level of anti-  
bacterial activity and can be modified as desired. The  
15 preferred antibacterial agent is 2-hydroxy-4,2',4'-trichloro-  
diphenylether (DP300). Other antibacterial agents are set out  
below. Many antibacterial agents, known to those skilled in  
the art and disclosed in e.g., US Patent Nos. 3,835,057 and  
4,714,563, both incorporated hereinbefore by reference, may be  
used.

#### Antimicrobials

Suitable antibacterial agents which may be used in the subject  
invention include:

25 2-hydroxy-4,2',4'-trichlorodiphenylether (DP300);  
2,6-dimethyl-4-hydroxychlorobenzene (PCMX);  
3,4,4'-trichlorocarbanilide (TIC);  
3-trifluoromethyl-4,4'-dichlorocarbanilide (TFC);  
2,2'-dihydroxy-3,3',5,5',6,6'-hexachlorodiphenylmethane;  
30 2,2'-dihydroxy-3,3',5,5'-tetrachlorodiphenylmethane;  
2,2'-dihydroxy-3,3',dibromo-5,5'-dichlorodiphenylmethane;  
2-hydroxy-4,4'-dichlorodiphenylether;  
2-hydroxy-3,5',4-tribromodiphenylether; and  
1-hydroxyl-4-methyl-6-(2,4,4-trimethylpentyl)-2(1H)-pyridinone  
35 (Octopirox).

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Other suitable materials include:

Benzalkonium chloride;  
Benzethonium chloride;  
5 Carbolic acid;  
Cloflucarbon (Irgasan CF3;4,4'-dichloro-3(trifluoromethyl)  
carbanilide);  
Chlorhexidine (CHX; 1,6-di(4'-chlorophenyl-diguanido)hexane);  
Cresylic acid;  
10 Hexetidine (5-amino-1,3-bis(2-ethylhexyl)-5-  
methylhexahydropyrimidine);  
Iodophors;  
Methylbenzethonium chloride;  
Povidone-iodine;  
15 Tetramethylthiuram disulfide (TMTD; Thiram); and  
Tribrominated salicylanilide.

In addition to a mild surfactant compound or compounds, the pH  
buffering compound or compounds; water and optionally (or as  
20 required in one embodiment), antimicrobial agent, the liquid  
skin cleansing compositions may contain optional components.

Optional components include organic solvents, such as ethanol;  
thickeners, such as carboxymethylcellulose, magnesium aluminum  
25 silicate, hydroxyethylcellulose, methylcellulose or carbopols;  
perfumes; sequestering agents, such as tetrasodium  
ethylenediaminetetraacetate (EDTA), EHDP or mixtures in an  
amount of 0.01 to 1%, preferably 0.01 to 0.05 wt%; coloring  
agents, opacifiers; and pearlizers such as zinc stearate,  
30 magnesium stearate, TiO<sub>2</sub>, EGMS (ethylene glycol monostearate)  
or Lytron 621 (Styrene/Acrylate copolymer); all of which are  
useful in enhancing the appearance or cosmetic properties of  
the product.

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The following preservatives may also be used in the liquid skin cleansers of the invention:

LIQUID SKIN CLEANSER PRESERVATIVES

5	<b>PRESERVATIVE</b>	<b>CHEMICAL NAME</b>
	Bronopol	2-Bromo-2-nitropropane-1,3,diol
10	Dowicil 200	cis Isomer of 1-(3-chloroallyl)-3,5,7-triaza-1-azoniaadamantane-chloride or Quaternium 15
15	Glycacil	3-Iodo-2-propynyl butyl carbamate
	Glydant XL 1000	DMDM Hydantoin or dimethyloldimethylhydantoin
20	Glydant Plus	DMDM Hydantoin and 3-Iodo-2-propynyl butyl carbamate
	Formaldehyde	Formaldehyde
25	Germall 11	N-(Hydroxymethyl)-N-(1,3-dihydroxymethyl-2,5-dioxo-4-imidazolidinyl)-N'-(hydroxymethyl) urea or Diazolidinyl urea
30	Germall 115	N,N'-methylene-bis-[N'-1-(hydroxymethyl)-2,5-dioxo-4-imidazolidinyl]urea or imidazolidinyl urea
	Glutaraldehyde	Glutaraldehyde

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- 5           Kathon CG           Mixture of 5-chloro-2-methyl-4-isothiazoline-3-one- and 2-methyl-4-isothiazoline-3-one or a mixture of methyl, chloromethyl isothiazolinone and methyl isothiazolinone
- 10           Parabens           Methyl Paraben, and Ethyl Paraben, Propyl Paraben and Butyl Paraben or those esters of p-hydroxybenzoic acid
- Phenoxyethanol       2-Phenoxyethanol
- Salicylic Acid       Salicyclic Acid or o-Hydroxybenzoic acid
- 15           Sorbic Acid           Sorbic Acid, Potassium Sorbate
- Coconut acyl mono-or diethanol amides as suds boosters, and strongly ionizing salts such as sodium chloride and sodium sulfate may be used to advantage.
- 20           Antioxidants such as, for example, butylated hydroxytoluene (BHT) may be used advantageously in amounts of about 0.01 wt% or higher, if appropriate.
- 25           Cationic conditioners which may be used include Quatrisoft LM-200 (Polyquaternium-24); polyethylene glycols such as
- Polyox           WSR-205           PEG 14M,  
                          WSR-N-60K          PEG 45M, or  
30                        WSR-N-750          PEG 7M; and
- Merquat Plus 3330 - Polyquaternium 39.

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Thickeners which may be used include Americoll Polymer HM 1500 (Nonoxynyl Hydroethyl Cellulose); Glucan DOE 120 (PEG 120 Methyl Glucose Dioleate).

5 Unless stated otherwise, the percentages in the specification, examples and claims are percentages by weight.

The invention will now be illustrated by way of the following non-limiting examples.

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#### FIGURES

Figure 1 shows the effect of addition of hexanoic acid on bactericidal activity.

15

Figure 2 shows the bactericidal activity of a liquid cleansing formulation containing 2 wt% fatty acids of varying chain length.

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Figure 3 shows the effect of the concentration of hexanoic acid on the bactericidal activity of a liquid cleansing formulation.

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Figure 4 shows the effect of pH on the bactericidal activity of the liquid cleansing formulation of example 1 in the presence and absence of 2 wt% hexanoic acid.

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Figure 5 shows the effect of 2 wt% hexanoic acid on the bactericidal activity of a range of commercially available skin cleansing products.

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Figure 6 shows the effect of 2 wt% fatty acid on the foam height of the liquid cleansing formulation of example 1.

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EXAMPLES

An in vitro Bactericidal Kill Test is used to measure antimicrobial activity in the examples which follow. Methodology for the test is set forth below:

IN VITRO BACTERICIDAL KILL TEST

An in vitro bactericidal test was used to determine the antibacterial effect of products on Staphylococcus aureus ATCC #6538 during a short contact time. One milliliter (about  $10^8$  cells) of bacteria was exposed for one minute to a one-percent solution of liquid skin cleansing composition. The sample was added to additional water, mixed, and further diluted in 0.1% peptone. Duplicate samples of appropriate dilutions were plated on neutralizing media. In addition, the bacterial culture was plated to determine the actual number of organisms inoculated. The plates were incubated at 34°C for 48 hours and enumerated. The CFU/ml (colony forming units per milliliter) from dilutions with plate counts in the range of 30-300 were averaged together to produce the final CFU/ml.

The results may be expressed as the log of the CFU/ml. The culture control indicates the actual number of bacteria inoculated while the water control reflects the number of organisms recovered in the absence of product. The lower the number, the more effective the solution was in killing the bacteria.

In this assay, a sampling error of approximately 0.5 log is likely, therefore differences of 0.5 log between products may not be significant. As a result, the data should be viewed in terms of trends rather than as absolute numbers.

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Example 1

Applicants tested the effect of 2% hexanoic acid in (1) water; a full liquid skin cleansing formulation, as set forth below, with and without Triclosan (DP300). The results are set forth in Figure 1.

The formulation used was as follows:

INGREDIENT	% BY WEIGHT
Acyl Isethionate	1-15%
Anionic other than Acyl Isethionate (SLES)*	1-15%
Amphoteric Surfactant**	5-15%
pH Buffering Compound (Hexanoic Acid)	1-5%
Sequestrant (EDTA or EHDP)	0.01-0.1%
Moisturizer (e.g. cationic polymer)	0.05-3.0%
Standard additives (e.g., dyes, perfumes)	0-10%
Water	Balance

\* Sodium lauryl ether sulfate

\*\* Cocamidopropyl betaine

As seen from Figure 1, hexanoic acid increases antimicrobial activity in the full formulation both with and without Triclosan.

Example 2Zein Solubilization AssayIn vitro "Mildness" Test/Assessing Mildness

It is generally believed that surfactants are irritants because they penetrate the stratum corneum and then react with the inner cells of the epidermis.

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Traditionally, the study of percutaneous absorption has focused on measuring the diffusion of chemicals through the stratum corneum.

5 We have obtained information on mildness potentials of the compositions of the invention through the use of in vitro tests which have been demonstrated to correlate well with in vitro tests.

10 Gotte in Proc. Int. Cong. Surface Active Subs., 4th Brussels (1964), 3, 83-90 and Schwinger in Kolloid-Z.Z.Poly., (1969), 233, 898 have shown that the ability to solubilize zein, an insoluble maize protein, correlates well with irritation potential.

15 More specifically, the greater the zein solubilization, the greater the irritation potential of a composition.

20 In order to test irritancy potential, a 1% solution (by weight active) of surfactant (30 mls) was added to 1.5 g zein and stirred at room temperature for one hour. Residual zein was collected by centrifugation and dried under vacuum to constant weight. Differences between starting and residual weights were used to calculate % zein dissolved.

25 The zein dissolution values for some skin cleansing formulations generally compared to soap are given below:

Soap (Ivory <sup>(R)</sup> )	82.4%
30 Dove <sup>(R)</sup> Beauty Bar	55.0%
Liquid Lever 2000 <sup>(R)</sup>	41.9%

35 Using the zein solubilization assay, the formulations of the invention all showed zein solubilization percentage well below that of soap. Specifically, the composition of Example 1 had

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solubility of about 28%. When octanoic acid was used, solubility was about 31%.

### Example 3

5 In order to see the effect of chain length on the antibacterial effect of the compound or compounds of the invention, applicants tested various saturated and unsaturated C<sub>2</sub> to C<sub>20</sub> fatty acids in the liquid cleansing formulation of example 1 to determine their effect. Results are set forth in Figure 2.

10 As can be seen from Figure 2, shorter chain length resulted in enhanced antibacterial effect. CFU stands for colony forming units and a decrease in CFU/ml is equivalent to greater antibacterial effect.

### Example 4

20 Hexanoic acid was added to the liquid cleansing formulation of example 1 at various concentrations to determine the concentration effect on antibacterial effect. The results are set forth in Figure 3.

25 As seen in Figure 3, an effect was seen at concentrations as low as 0.5%.

### Example 5

30 In order to determine the pH effect, hexanoic acid was added at various pH ranges to the formulation of example 1. The pH of the liquid cleansing formulation of example 1 was adjusted using IN HCl or NaOH.

35

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As seen in Figure 4, antibacterial effect is significantly enhanced at pH below 5.

Example 6

In this example the effect of hexanoic acid in commercially available compositions was tested. The results are set forth in Figure 5. Composition 1 was the composition of Example 1.

The estimated composition or list of ingredients for the commercially available compositions in Figure 5 is set forth below:

Composition 2Estimated % by Weight

Sodium Laurel Sulfate	4.5
Sodium Chloride	2.0
Quaternium - 15	1.7
Potassium Cohydrolyzed Collagen	1.7
Lauryl Polyglucose	1.6
Cocoamide MEA	0.4
Triclosan	0.24
Water	86.0

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Composition 3 (Estimated List of Ingredients)

	Triclosan
	Water
5	Sodium C <sub>14</sub> -C <sub>16</sub> Olefin Sulfonate
	Lauramide DEA
	Hydrolyzed Silk Protein
	Cocamidopropyl Betaine
	Polyquaternium -7
10	Aloe
	Glycerin
	EDTA
	Sodium Chloride
	Hydantoin
15	Dyes and Fragrances

Composition 4 (Estimated Ingredients)Estimated % by wt.

	Ammonium Lauryl Sulfate	6.6
20	Sodium Laureth Sulfate	5.2
	Lauramide DEA	3.5
	Glycerin	1.5
	Isostearamidopropyl Morpholine Lactate	0.6
	Citric Acid	0.2
25	Disodium Ricinoleamido MEA Sulfosuccinate	0.1
	Triclosan	0.2
	Water	80.9
	Dyes, EDTA, Hydantoin	

30



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Example 5a (Estimated Ingredients)

Chloroxylenol  
Water  
Sodium C14-16 Olefin Sulfonate  
5 Ammonium Lauryl Sulfate  
Linoleamide DEA  
Cocamide DEA  
Cocamidopropyl Betaine  
Sodium Chloride  
10 Glycerin  
Fragrance  
Disodium EDTA  
Citric Acid  
PEG-45M  
15 Methylchloroisothiazolinone  
Methylisothiazolinone  
Dyes

Example 5b (Estimated Ingredients)

20 Chloroxylenol  
Water  
Sodium C14-16 Olefin Sulfonate  
Lauramide DEA  
Silk Peptide  
25 Hydrolyzed Silk Protein  
Cocamidopropyl Betaine  
Poly-Quaternium-7  
Aloe Vera Gel  
Glycerin  
30 Tetrasodium EDTA  
Sodium Chloride  
DMDM Hydantoin  
Citric Acid  
Fragrance  
35 Dyes

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Example 5C (List of Main Ingredients)

Water  
 Propylene Glycol  
 5 Sodium Isethionate  
 Sodium Alkylbenzenesulfonate  
 Sodium Laureth Sulfate  
 Sodium Cocoyl Isethionate  
 Sodium Tallow/Coconut Soap  
 10 Methyl Paraben  
 Propyl Paraben  
 EDTA, EHDP  
 Fatty Acid  
 Sulfosuccinate

15

Example 5d (Estimated Ingredients)Estimated % by wt.

	Sodium Laureth Sulfate	6.8
	Sodium Lauryl Sulfate	5.0
20	Lauramide DEA	2.2
	Sodium Sulfate	2.6
	Cocamidopropyl Betaine	1.8
	Sodium Chloride	0.6
	Styrene/Acrylate Copolymer	0.8
25	Water	79.9
	Misc. (Octoxynel-9, DMDM Hydantoin, Tetrasodium EDTA, Citric Acid)	

30 As noted from the Figure, hexanoic acid works effectively in  
 various different compositions whether or not a germicide was  
 present.

- 25 -

Example 7

In order to determine whether the buffering compound or compounds of the invention had a negative effect on foam height, the composition of Example 1 was tested with various fatty acids. Foam height was measured by the method described in ASTM D1173-53 hereby incorporated by reference into the subject application. More particularly, foaming ability of 1% liquid skin cleansing formulations was measured by dripping 200 ml of the solution from Miles pipet onto 50 ml of the solution in a glass cylinder as specified in ASTM D1173-53. Foam height readings were taken after 1 minute at 25°C. As seen in Figure 6, foam height remained almost the same.

Example 8

The buffering compound or compounds of the invention may also be used in the following formulations.

FORMULATION A	
Component	% by weight
Sodium Isethionate	3-5%
Sodium Alkene Benzene Sulfonate	1-3%
Sodium Laureth Sulfate	3-5%
Sodium Cocoyl Isethionate	8-12%
Sodium Tallow/Coconut Soap	1-3%
Preservative (e.g., Methylparaben)	0.1-0.5%
Sequestrants	0.01-0.05%
Fatty Acid (e.g. Stearic Acid)	7-10%
Sulfosuccinate	3-5%
Water plus minors	to balance

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FORMULATION B	
Component	% by Weight
Sodium Cocoyl Isethionate	5-8%
Cocamidopropyl Betaine	5-8%
Sulfosuccinate	2-5%
Fatty Acid	6-9%
Sodium Isethionate	1-3%
Silicone Emulsion	3-7%
Sequestrant	0.01-0.05
Water plus minors	to balance

5

10

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CLAIMS

1. A skin cleansing composition comprising:

5           (1) 1 to 99 wt% of a surfactant system comprising one or more surfactants which alone or together are milder than soap itself when measured by percent of zein dissolved.

10           (2) 0.1 to 10 wt% of compound or compounds which buffers the pH of the composition such that the pH is no higher than 5.5 upon dilution with water at ranges of 1:0.5 to 1:100 dilution; and

15           (3) 1 to 99 wt% water.

2. A composition according to claim 1 further comprising 0.001 to 5 wt% of an antibacterial agent.

20           3. A composition according to claim 1 or 2, wherein the surfactant system is 2-85 wt% of the composition.

4. A composition according to claim 3, wherein the pH is from about 3.0 to 5.0.

25           5. A composition according to claims 1 or 2, wherein the pH buffering compound is selected from of organic acids, organic acid anhydrides and inorganic acids.

30           6. A composition according to claim 5, wherein the inorganic acid is selected from phosphoric and carbonic acid.

35           7. A composition according to claim 5, wherein the organic acid is selected from carboxylic acids, hydroxy carboxylic acids and polymeric acids.

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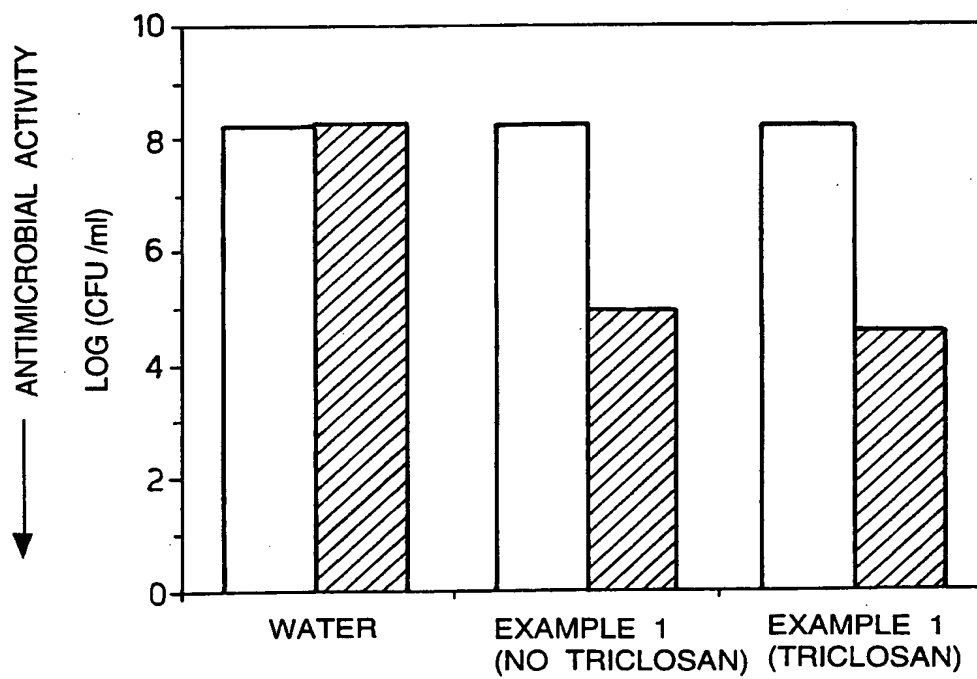
8. A composition according to claim 7, wherein said  
polymeric acid is a polymer containing carboxylic acid or  
anhydride with weight average molecular weight of at  
least 3000 and a mole % carboxyl functionality of at  
least 40%.
9. A composition according to claim 8, wherein the polymeric  
acid is selected from the group consisting of polyacrylic  
acid, polymethacrylic acid, pectic acid and mixtures  
thereof.
10. A composition according to claim 7, wherein the  
carboxylic acid is a substituted or unsubstituted  $C_2$  to  $C_{18}$   
fatty acid.
11. A composition according to claim 7, wherein the hydroxy  
carboxylic acid is lactic acid.
12. A composition according to claim 1 or 2, wherein the  
surfactant system comprises 1 to 15 wt% acyl isethionate.

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Fig.1.

□ NO HEXANOIC ACID  
PRESENT

▨ 2% HEXANOIC ACID  
PRESENT



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Fig.2.

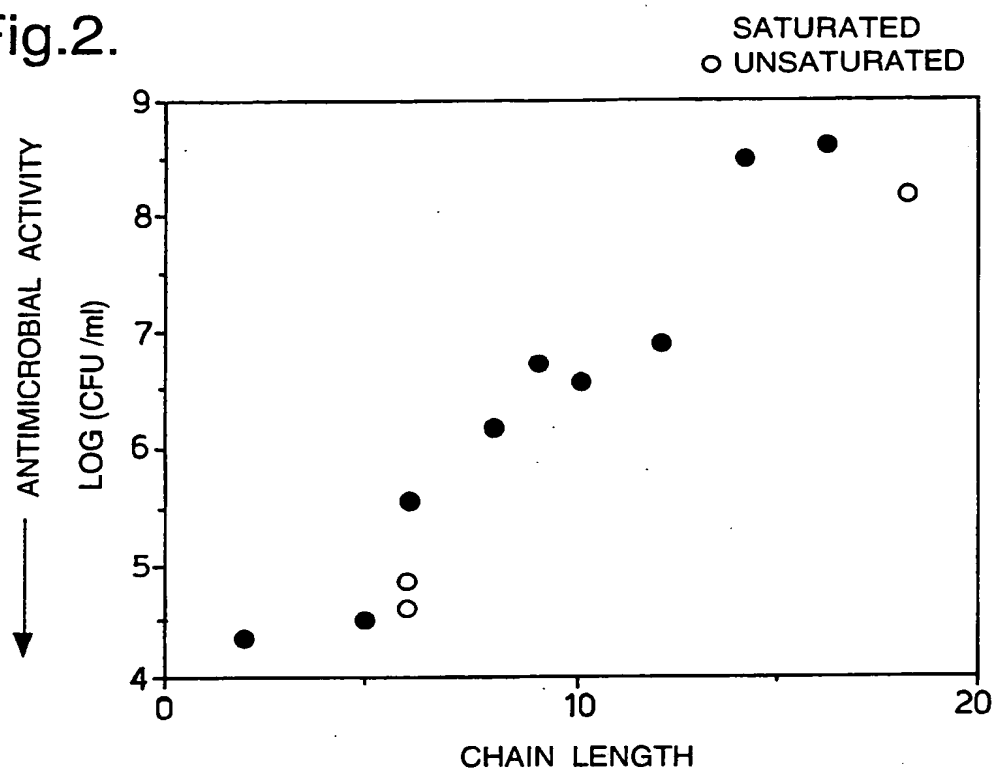
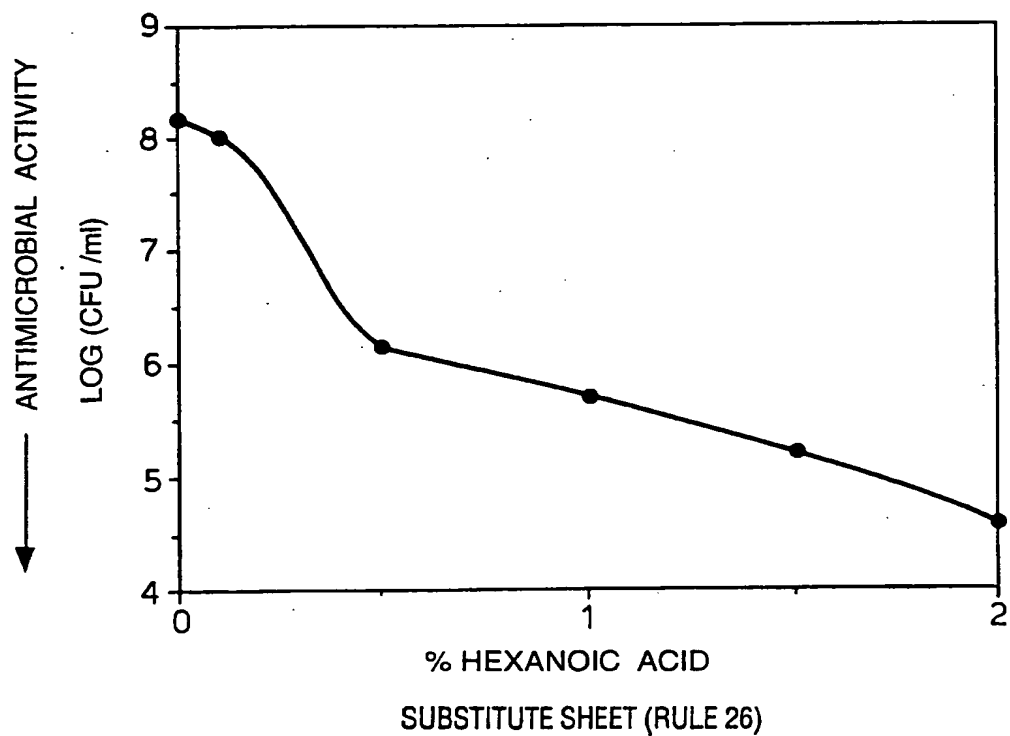


Fig.3.





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Fig.4.

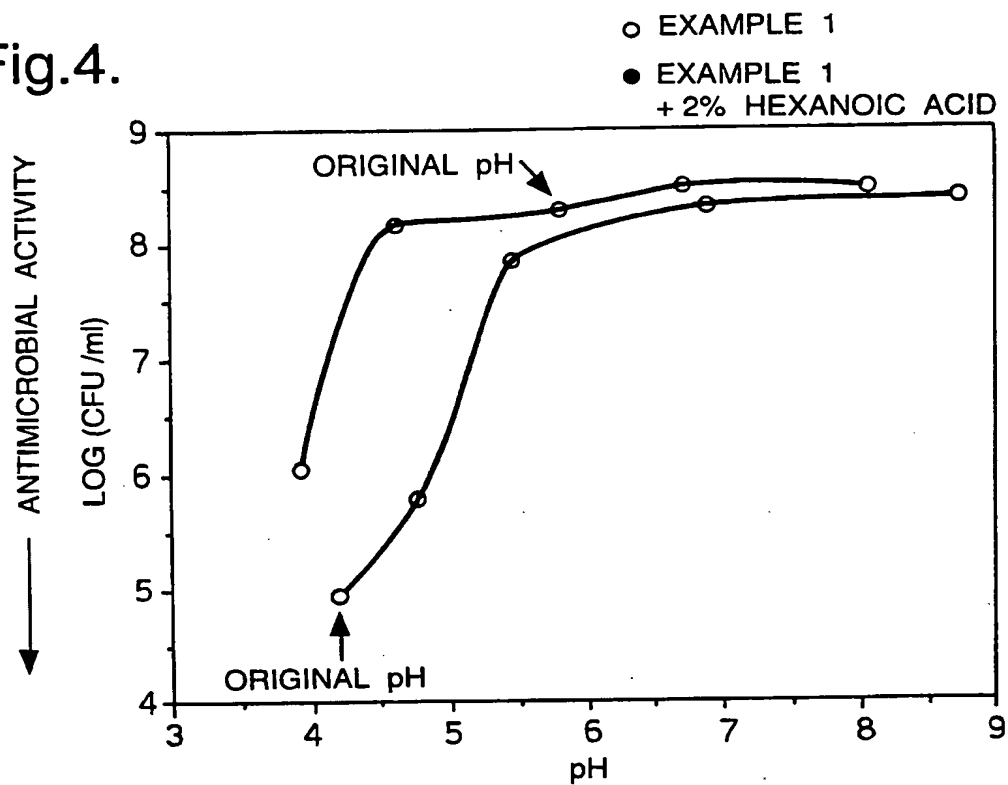


Fig.6.

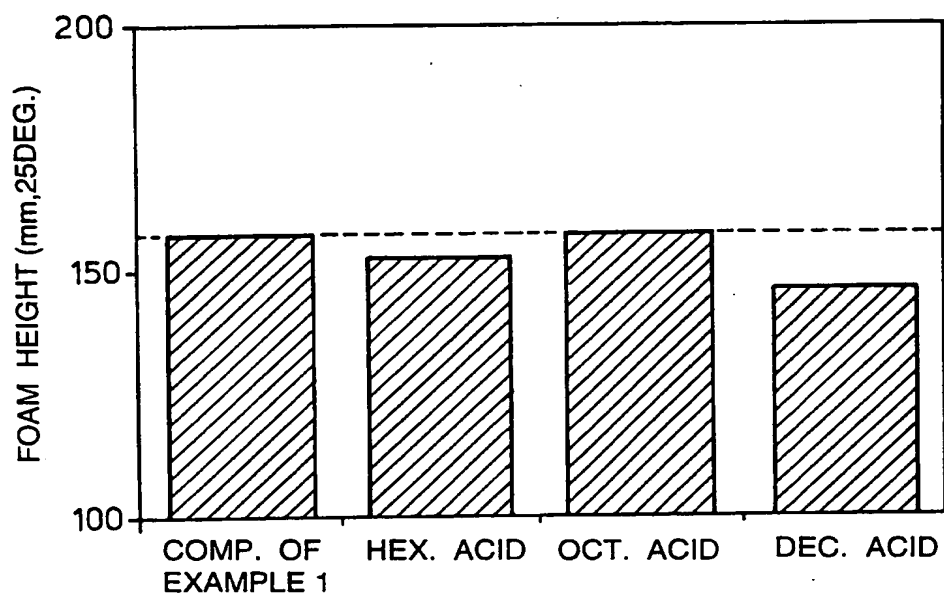
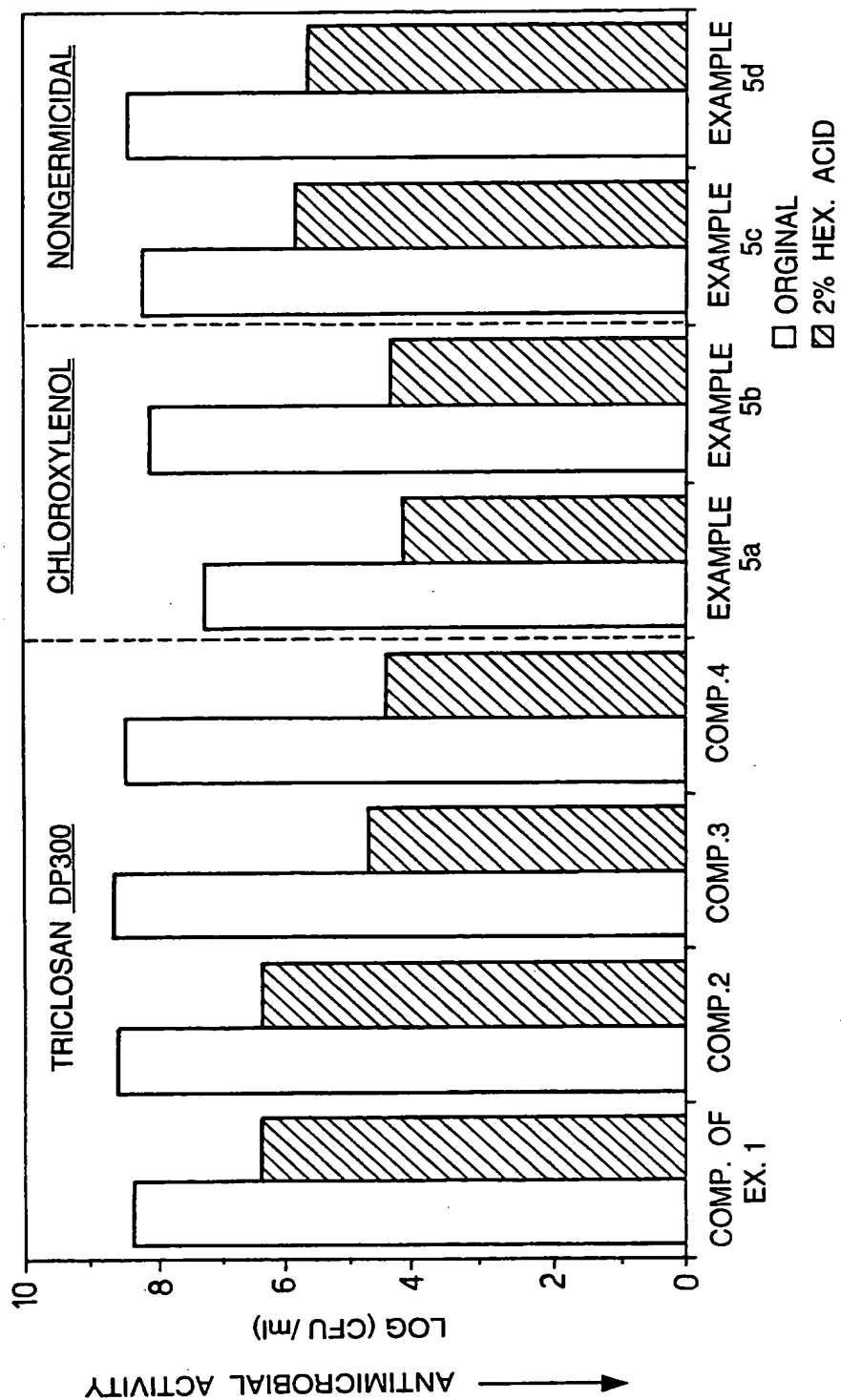


Fig.5.



# INTERNATIONAL SEARCH REPORT

Intern. Application No  
PCT/EP 95/01944

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61K7/50

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO,A,94 18292 (THE PROCTER & GAMBLE COMPANY) 18 August 1994 see the whole document ---	1-3,7, 11,12
X	WO,A,92 18100 (THE PROCTER & GAMBLE COMPANY) 29 October 1992 cited in the application see the whole document ---	1-6
X	WO,A,91 09923 (THE PROCTER & GAMBLE COMPANY) 11 July 1991 see the whole document ---	1-3,5,7, 10,12
X	EP,A,0 024 031 (STERLING GRUG INC.) 18 February 1981 see the whole document ---	1-3,5,7
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Date of the actual completion of the international search

13 October 1995

Date of mailing of the international search report

27. 10. 95

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 95/01944

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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PCT/EP 95/01944

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**PCT/EP 95/01944**

Form PCT/ISA/210 (patent family annex) (July 1992)